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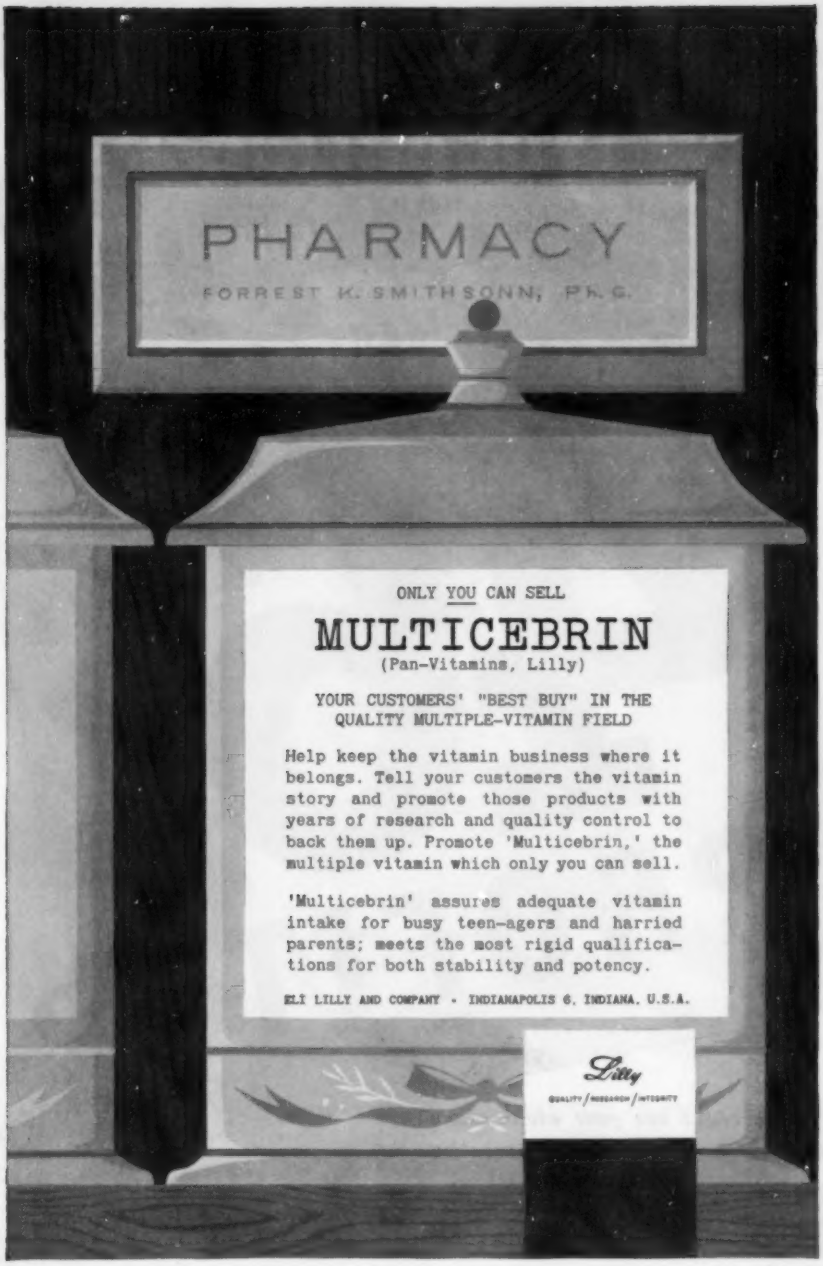
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IN MEMORIAM

EARL R. SERLES

THE death of Dr. Earl R. Serles marks the passing of one of Pharmacy's leading statesmen and educators. Dr. Serles, who was Dean of the University of Illinois College of Pharmacy, began his career in pharmacy in 1909 when he enrolled as a pharmacy student at South Dakota State College. His education continued through the Ph.D. degree which he earned at the University of Minnesota, majoring in Pharmacology. Dr. Serles became the Dean at the University of Illinois in 1940 after having been at South Dakota State College for a number of years as Head of the Division of Pharmacy. Under his leadership, the College of Pharmacy at the University of Illinois made great progress and, in September 1954, he saw the accomplishment of one of his fondest hopes realized when the University opened what is probably the largest and most modern new building in the United States devoted to the teaching of pharmacy. The work and effort required in planning this new building and bringing those plans into fulfillment undoubtedly exacted a toll and may have shortened his life.

Dr. Serles during his life was very active in both the American Association of Colleges of Pharmacy and the American Pharmaceutical Association and he served as President of each of these national organizations. His work on the campus of the University of Illinois led to many responsibilities including certain periods of service as Chief Executive Officer of the University's professional colleges.

One could recite at length the many contributions and achievements of Dr. Serles during his lifetime for they were numerous and impressive. Dr. Serles was not only a leader and an executive but he knew how to get things done. In the fullest sense of the word, he devoted his life to the profession. Meetings of educators in pharmacy and those meetings of the A.Ph.A. will not be quite the same now that he is gone, but his influence on these groups and on the whole of American Pharmacy will long endure.

EDITORIAL

WORLD POPULATION AND THE FUTURE

WE were very much impressed by an article titled "Our Reproductive Potential" written by Fairfield Osborn and published in a recent number of *Science*. While we are surely not expert in assessing the long-term effects of the staggering increase in world population which is predicted, it is possible by simply observing changes which have taken place in the last few decades to appreciate some of the problems outlined by this author. Dr. Osborn cites figures which are difficult for the ordinary man to grasp; for example, during the last one hundred years, the world's population has increased from 1200 million to 2400 million but, in the last ten years alone, world population has increased by 300 million. As he points out, it is principally the progress of medical science and public health measures which have brought this about.

The three factors which at one time operated to keep population in check were starvation, disease, and war. History gives us ample evidence that, when the population pressure within a country becomes sufficiently great, the likelihood of an invasion of some other country having more space and raw materials is a threat to world peace. This was, indeed, the reason that Italy attacked Ethiopia and basically the reason that Japan felt it imperative to take the steps leading to its involvement in World War II. For example, in Japan—a country about the size of the State of Montana, the population increased from 47,000,000 in 1900 to 73,000,000 in 1940. Even today in Japan, the population growth is not adequately checked in spite of the fact that abortions are estimated to equal the number of live births each year. While we terminated the invasion of the mainland by Japan when we conquered her in the last war, we did not correct her basic difficulty and we have had to support her economy since the end of the war. Even now, we are forced to alter our ban on her trade with Red China since we realize that her economic condition cannot be made sound unless raw materials from the mainland are available for Japanese industry and it is permitted to send back manufactured goods.

The present situation in Egypt is caused primarily by the country's inability to support 23,000,000 people where there are only

about 13,000 square miles of arable land. Such people who are on the verge of starvation give ready support to any political leader who offers even the slightest hope of improved conditions. Even in Red China where one would expect the Marxist philosophy to prevail, their leaders have been forced to adopt certain "reactionary" policies concerning population growth which Karl Marx would have abhorred. The Chinese leaders have found that their efforts to raise the economic level and educational standards of their 600,000,000 people is almost nullified by the population increase of two per cent a year.

We in the United States are inclined to consider unrestrained population growth as something peculiar only to the "underdeveloped" countries. In the first place, we have, right here in our own country, a rate of increase greater than that in either China or India. As Osborn points out, our prevailing attitude is one of taking it for granted that such an increase is desirable. The talk of "more sales", "expanded markets", and ever higher "standards of living" is beginning to be questioned by certain economic experts. The thing which seems to be the greatest threat to our future, if our population continues to grow, is whether we will be able to supply them with the material things which they will want or need. At the present time, with less than ten per cent of the free world's population and only eight per cent of its land area, the United States consumes about one-half the free world's volume of goods. In many respects, we have become a "have-not" nation and are dependent upon others for our raw materials. There is a serious doubt in the minds of many whether we can continue indefinitely to outbid and outconsume all other people in the world. There are clear signs that many of the less fortunate people of the world are no longer content to have most of the world's goods consumed by the American colossus, particularly when many of these products as raw materials originate in their own country.

The most serious future threat of all here in the United States is the social and political impact which population growth will have. Everyone must stop and think what our environment and what our cultural, psychological, and social condition will be when there are 100,000,000 more people. Was man ever intended to live under the conditions of social crowding and with as little free choice as further

herding together in cities and suburbs will produce? Will not the time come when quiet and solitude will be things of the past? And yet, are not these things essential to the mental and spiritual welfare of everyone?

We shall not discuss what steps, if any, could be or should be taken in facing the problem of over-population either here in the the United States or in the world at large. It is a very complex problem and one which involves many social and religious considerations which are difficult, to say the least. It is time, however, that this, the greatest problem facing the human race, be given the attention it deserves and there are signs of an increasing awareness of its implications even in the United Nations for, indeed, world peace itself can never be attained without some appropriate steps. Most of all, we should be concerned, each of us, with the kind of world which will be inherited by our children and our children's children. It should be the kind of world in which we ourselves would be happy to live.

L. F. Tice

CARBOPOL 934 AS A BASE FOR PHARMACEUTICAL JELLIES

By Phyllis M. Caver,[1] Joe Gregorio [2] and W. Lewis Nobles [3]

CARBOPOL 934 [a] is a white, free flowing, acidic polymer which readily disperses in water to yield a low viscosity acid solution. Upon neutralization, a clear stable gel results. Previous reports (1-4) have pointed out some of the potential applications of this product in cosmetic and pharmaceutical formulations.

Previously, it has been indicated that Carbopol gels are not susceptible to hydrolysis or polymeric degradation due to bacterial and/or fungal attack (5). In connection with this work, several of the jellies were allowed to come into contact with airborne molds. In those cases in which the concentration of Carbopol was 3% or less, the mold growth continued for a period of time, which might be dependent on the nutritional value of the air entrapped in the mucilage. This growth was not noted with preparations containing more than 3% Carbopol. It should be emphasized that in no case were gels subject to polymeric degradation due to the mold growth. If the mold were dependent upon Carbopol 934 as a source of nutrition, however, degradation should certainly ensue and with it would be a marked alteration of the rheological properties of the system. This was not observed in any case. Certainly, the presence of mold is feasible so long as the carrier (in this case, a mucilage based on Carbopol 934) is non-toxic to the mold. Thus, the Carbopol 934 mucilage may be considered as an inert carrier. Other observations of such mold contamination have been made and are in accord with the above results (6).

In recent years, emulsion and/or washable ointment bases have achieved a high degree of popularity in dermatological practice for several reasons. Some of these are:

---

1. Instructor, School of Pharmacy, University of Mississippi.

2. Senior student, School of Pharmacy, University of Mississippi.

3. Professor of Pharmacy and Pharmaceutical Chemistry, University of Mississippi.

a. Samples supplied through the courtesy of B. F. Goodrich Chemical Company, Cleveland, Ohio.

1. Ready absorption of the medicament from the skin.
2. Non-greasiness of the base.
3. Ease of removal of the excess ointment from the surface to which it has been applied by washing.

Pharmaceutically, jellies should manifest these same properties. Consequently, it appeared to be of interest to compare various gelling agents and to attempt to determine the compatibility—or lack of it—of commonly used dermatological medications with these agents. Recently, Hutchings and Singiser (7) and Kaufman, Burlage and Lloyd (8) reported the results of their work in this area. Previously (4), we reported some preliminary observations concerning the uses of Carbopol 934 as a dermatological vehicle. The results of this earlier work were so encouraging that we should like to report at this time on the extension of these earlier studies. In general, the methods of preparation of the bases and incorporation of the medicinals are similar to those previously described (4).

This work may be divided into two main categories: (a) comparison of the properties of Carbopol gels with other substances commonly used as jelly bases and (b) a study of the compatibility of medicinals commonly prescribed in dermatology with Carbopol. The results of (a) are indicated in Table I and those of (b) in Table II.

In every case, the jellies were easily prepared, elegant in appearance and all those that are indicated as being compatible remained elegant in appearance and stable at room temperature throughout the test period of 40 days. When these preparations are applied to the skin, they rub in well and do not leave a greasy, sticky feel. They are easily removed by washing with soap and water.

Summary

Certain pharmaceutical properties of jellies utilizing Carbopol 934 were compared with those of other commonly used jelly bases. In every concentration employed, the color, viscosity, and spreadability of Carbopol jellies were satisfactory.

Seventeen commonly prescribed dermatological agents were successfully incorporated into jellies prepared from Carbopol. It was not possible to incorporate phenol and resorcinol successfully into this type of jelly base.

TABLE I

PHARMACEUTICAL PROPERTIES OF THE JELLIES

Gum [a]	Concentration of Gum, %	Color	pH 5% Solution of Jelly	Viscosity	Spreadability	Odor
1. Kelgin LV	7	Light Amber	7	Satisfactory	Fair	Slight
2. Kraystay T	4	Light Tan	7	Satisfactory	Satisfactory	Very Faint
3. Methocel 400	3	Clear	8	Satisfactory	Fair	Very Faint
4. Jaguar Gum	2	Pale Gray	6	Excellent	Satisfactory	Undesirable
5. Carbopol 934	2	Clear	6-7	Excellent	Satisfactory	Faint Musty
6. Carbopol 934	3	Clear	6-7	Excellent	Satisfactory	Faint Musty
7. Carbopol 934	5	Clear	6-7	Satisfactory	Satisfactory	Faint Musty

a. Most of this—plus additional—information of numbers 1-4 may be found in reference number 5 at the end of this article.

TABLE II

COMPATIBILITY OF CARBOPOL GEL WITH VARIOUS THERAPEUTIC AGENTS

Active Ingredient	% Active Ing.	Carbopol Base	% [b]
Ammoniated Mercury [a]	5	Compatible	2
Aureomycin [a]	3	Compatible	5
Benzoic Acid [a]	12		
Salicylic Acid	6	Compatible	5
Cade Oil	3	Compatible	4
Cade Oil	5	Compatible	4
Chrysarobin [a]	6	Compatible	2
Coal Tar [a]	5	Compatible	4
Coal Tar Solution	5	Compatible	4
Ephedrine Sulfate	1	Compatible	4
Ethylaminobenzoate [a]	1	Compatible	2
Ichthammol	3	Compatible	4
Iodine [a]	4	Compatible	4
Methylrosaniline Chloride	1	Compatible	5
Penicillin [a]	1000 units/Gm Ointment	Compatible	4
Phenol	2	Incompatible	4
Resorcinol	3	Discoloration	4
Salicylic Acid	3	Compatible	4
Sulfathiazole [a]	5	Compatible	4
Sulfur [a]	20	Compatible	2
Vioform	3	Compatible	4

a. Previously reported. See reference number 4.

b. Various percentages of Carbopol were used. Those indicated appear to yield the most elegant product.

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(2) Streeter, Ruth E., Caver, Phyllis M. and Nobles, W. L., *ibid.,* 671 (1955).

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(4) Nobles, W. L., *Drug and Cosmetic Industry 77,* 178 (1955).

(5) "Carbopol 934—Service Bulletin GC-20", B. F. Goodrich Chemical Company, Cleveland, Ohio.

(6) Private communication—Mr. L. L. Shailer, B. F. Goodrich Chemical Company.

(7) Hutchins, H. and Singiser, R. E., *J. Am. Pharm. Assoc., Pract. Pharm. Ed. 16,* 226 (1955).

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A STUDY OF THE HYPOTENSIVE AND EMETIC EFFECTS OF 2-METHYL-5,8-DIMETHOXYCHROMONE [1]

By G. Victor Rossi and Amiram Lifschitz

KHELLIN, a crystalline, biologically active compound isolated from the fruit of the plant Ammi visnaga, has been used extensively since 1949 for the prophylaxis and treatment of angina pectoris, and to a lesser extent for the relief of bronchial asthma. Although the clinical value of khellin remains controversial, most investigators agree that its therapeutic usefulness is markedly limited by the incidence and severity of the associated undesirable reactions, particularly nausea and vomiting.

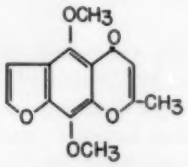
Many congeners of khellin, which chemically is 2-methyl-5,8-dimethoxyfuranochromone, have been synthesized and pharmacologically evaluated in an attempt to improve the vasodilatory activity and reduce the troublesome side effects. Jongebreur described the relationship between chemical structure and biological activity (1), together with the cardiovascular effects (2) of some of the synthetic pyrones and khellin. He reported the compound 2-methyl-5,8-dimethoxychromone (hereafter abbreviated as compound 2-5-8), which differs from khellin in that it lacks the furan group attached at positions 6 and 7, to approximately equal khellin in its ability to increase the rate of flow through the coronary blood vessels.

Doses of khellin which appreciably augment coronary flow exert no significant effect on the arterial blood pressure of anesthetized normotensive animals. Larger doses of khellin, and most of the synthetic chromones, elicited an immediate but transient drop in blood pressure when injected intravenously, whereas compound 2-5-8 produced a fairly sustained level of hypotension.

There remains a critical need for an orally effective antihypertensive agent providing prolonged moderate reduction of blood pressure unaccompanied by unpleasant or toxic reactions. On this basis we considered that it would be desirable to further investigate the

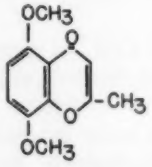
1. Received from the LaWall Memorial Laboratory of Pharmacology and Biochemistry, Philadelphia College of Pharmacy and Science, Philadelphia, Penna.

hypotensive effect of compound 2-5-8[2] in a variety of laboratory animals. Considering the prominent side effects of khellin, it was also our intention to evaluate the emetic potential of the related compound 2-5-8.



2-METHYL-5,8-DIMETHOXY-FURANOCHROMONE

KHELLIN



2-METHYL-5,8-DIMETHOXY-CHROMONE

Experimental

The blood pressure reducing effect of compound 2-5-8 was determined in anesthetized intact dogs and cats and in unanesthetized hypertensive rats. Mongrel dogs of both sexes, weighing from 6 to 8 Kg., and cats of both sexes, weighing from 2.5 to 4 Kg. were used. Both dogs and cats were fasted for 12 hours before each experiment and anesthetized with 30 mg./Kg. of sodium pentobarbital injected intraperitoneally. Blood pressure was recorded directly by means of a mercury manometer connected to a cannulated carotid artery with polyethylene tubing. Respiration was recorded with the aid of a tambour attached to a chest pneumograph. Intravenous injections were made into the femoral vein and a rubber catheter was used to introduce compounds into the stomach.

Hypertension was induced in male Sherman rats weighing approximately 125 Gm. by applying a figure-8 ligature made with coarse thread to one kidney stripped of fascia, removal of the contralateral kidney two weeks later, and subcutaneous implantation of a single 75 mg. pellet of desoxycorticosterone acetate.[3] All animals were maintained in constant temperature quarters with free access to Rockland Rat Diet and tap water. Following oral administration of

2. Generously supplied by Dr. Gustav J. Martin, Research Director of the National Drug Co., Philadelphia, Penna.

3. The authors wish to acknowledge the cooperation of Mr. Sidney Goldstein in providing the hypertensive rats used in this study.

compound 2-5-8 the blood pressure was determined every 30 minutes for 4 hours by the photoelectric tensometer method (3), incorporating minor modifications which have increased accuracy and ease of performance. Over this period of time the blood pressure of control groups, composed of an equal number of experimental animals receiving only distilled water, did not change significantly.

The emetic effect of compound 2-5-8 was determined by administering increasing doses orally to intact unanesthetized dogs and grading the response subjectively on the following basis: no effect (0), slight to moderate retching (+), severe retching without emesis (++), severe retching and vomiting (+++). The protection provided by 2 mg./Kg. of chlorpromazine (Thorazine) injected subcutaneously 30 minutes before the administration of compound 2-5-8 was also examined.

Results and Discussion

The hypotensive action of 2-methyl-5,8-dimethoxychromone in anesthetized intact dogs and cats and unanesthetized hypertensive rats is summarized in Table 1. Intravenous injection of 5 to 15 mg./Kg. of compound 2-5-8 in dogs resulted in a drop in blood pressure which was rapid in onset, of moderate intensity but of relatively short duration. Considerably larger oral doses were required to elicit comparable depressor effects. Compound 2-5-8 administered orally in doses of 25 to 50 mg./Kg. reduced blood pressure 10 to 30 mm. Hg gradually over a period of approximately 60 minutes and maintained the depressed level from 3 to 5 hours. Larger doses increased somewhat the degree of hypotensive response but to a greater extent, prolonged the duration of action. Cats responded in a qualitatively similar manner, but were considerably more sensitive than dogs to the blood pressure reducing effects of the compound.

The rats selected for this study from our colony of hypertensive animals all exhibited systolic blood pressures of 200 mm. Hg or greater. Hypotensive effects obtained in the rat were somewhat greater in degree but markedly shorter in duration than those produced by comparable doses of compound 2-5-8 in the dog. In all three species examined (dog, cat and hypertensive rat), inordinately large doses of compound 2-5-8 were needed to evoke consistent and moderately prolonged decreases in arterial pressure. The magnitude of the doses required would appear to preclude 2-methyl-5,8-dimethoxychromone as a potentially useful antihypertensive agent.

TABLE 1

HYPOTENSIVE EFFECT OF 2-METHYL-5,8-DIMETHOXYCHROMONE

Experimental Animal	No. of Animals	Route of Administration	Dose mg./Kg.	Mean Drop in B.P. mm. Hg.
Dog	5	intravenous	15	37
"	2	oral	25	10
"	5	"	50	30
"	5	"	75	35
"	2	"	100	55
Cat	4	"	25	40
"	2	"	50	88
Hypertensive rat	12	"	25	20
"	21	"	50	31
"	10	"	75	57

Although the production of nausea can only be evaluated in the clinic, a valuable estimation of the emetic potential of drugs can be obtained by observing their effects in experimental animals. Administration of increasing doses of compound 2-5-8 via stomach tube to unanesthetized dogs established the threshold emetic dose to be 25 mg./Kg. in this species (Table 2). This dose consistently produced symptoms of depression, confusion, disorientation, ataxia, and paralysis of the hind legs, together with severe retching, vomiting and defecation. The characteristic syndrome also followed oral doses of 30, 50 and 75 mg./Kg. Subcutaneous injection of 2 mg./Kg. of chlorpromazine 30 minutes prior to administration of compound 2-5-8 provided partial, but in no case complete, protection against the emetic effects of the latter agent in doses as large as 75 mg./Kg.

The synthetic compound 2-methyl-5,8-dimethoxychromone, in contrast to the naturally-occuring coronary dilator 2-methyl-5.8-dimethoxyfuranochromone (Khellin), possesses significant hypotensive activity in the dog, cat and rat. However, the doses necessary for consistent, moderate and prolonged reduction of blood pressure in these species also evoke a variety of untoward reactions, especially referable to the central nervous system and gastrointestinal tract, in the unanesthetized animal.

TABLE 2

EMETIC EFFECT OF 2-METHYL-5,8-DIMETHOXYCHROMONE IN THE UNANESTHETIZED DOG

No. of Animals	Dose of Compound 2-5-8 mg./Kg., p. os	Dose of Chlorpromazine* mg./Kg., s.c.	Response**
1	5	—	0
1	10	—	0
1	15	—	0
1	20	—	+
3	25	—	+++
3	25	2	+
1	30	—	+++
1	30	2	++
1	50	—	+++
1	50	2	++
1	75	—	+++
1	75	2	+++

* Administered 30 minutes prior to compound 2-5-8.

** No effect (O), slight to moderate retching (+), severe retching without emesis (++), severe retching and vomiting (+++).

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(3) Kersten, H., Grosene, W. G., Jr., Ablondi, F. and Subba Row, Y., *J. Lab. Clin. Med., 32,* 1090 (1947).

DRUG INFORMATION SOURCES

(Belgium and Germany)

BELGIUM

Recueil des Specialités Pharmaceutiques Médicales, by Revar. Liège, Maison DeSoer, 1946. 572 pp.

A handbook in four parts: I, A list of drugs (by proprietary name) sold in Belgium, with name of manufacturer or distributor. II, Description of specialty drugs, in alphabetic order, with detailed composition, indications, actions, dosage, price, name and address of manufacturer and his agent in Belgium. III, An index of specialty drugs according to principal therapeutic indications. IV, Alphabetic list of laboratories with their products and names and addresses of their agents in Belgium. Publisher's address: 21 Rue Ste. Veronique, Liège.

Le Compendium Médical; Formulaire des Specialités Pharmaceutiques. 2d ed. Brussels, Editions Documentaires Médico-Pharmaceutiques, Publi-Specia, 1948. 381 pp. 150 fr.

Proprietary-name list with composition, indications, dosage and form dispensed, but not always a clue to manufacturer of specific product. A new edition is expected to be published at the end of 1957.

Association Pharmaceutique Belge. Tarif des Specialités Pharmaceutiques. 1956 ed. Brussels, 1956. Various pagings (approx. 800 pp.) 500 fr.

The only official price list in Belgium, this handbook has three parts: I, A list of drugs by trade name with prices (by form supplied, i.e., tablets, etc.). Prices are official prices and reimbursement, if any, is mentioned. II, List of manufacturers with names of their products. III, List of laboratories and distributors with their addresses and telephone numbers. It is kept up-to-date by monthly supplements and revised annually. Publisher's address: 11 Rue Archimède, Brussels.

Annuaire de la Santé Publique et des Institutions Sanitaires, 1956-1957. Brussels, Agences de Publicité Denis Bodden & Dechy Réunies, 1957. 1258 pp. 425 fr.

A 240-page section on pharmaceutical specialties, arranged alphabetically by proprietary or common name, reports composition, available forms, manufacturers and sometimes indications for products of firms advertising in *l' Annuaire*. A list of manufacturers with their addresses is also included. Fully half the book is directory information for public health institutions, Red Cross, hospitals, physicians, medical specialists, pharmacists and insurance companies of Belgium and the provinces. Publisher's address: 67 Rue du Lombard, Brussels.

Compiler's note: Francs throughout are *Belgian francs*.

GERMANY

West Germany

Hagers Handbuch der Pharmazeutischen Praxis für Apotheker, Arzneimittelhersteller, Drogisten, Arzte und Medizinalbeamte, revised by Dr. G. Frerichs, G. Arends, Dr. H. Zörnig. Berlin, Springer Verlag.

Band I. 1573 pp. 1938; reprinted 1949. DM 75.—
Band II. 1579 pp. 1938; reprinted 1949. DM 75.—
Band III. (Ergänzungsband). 1610 pp. 1944; reprinted 1949. DM 75.—

Although old, this comprehensive reference work on chemical and botanic drugs is highly useful. Most of the text consists of monographs on medicinal substances arranged alphabetically by their Latin names. Drugs with related chemical structures, salts of a single element or alkaloids of one plant are found grouped in single monographs. Monographs give alternate names and detailed description, identification, chemical formula (frequently structural), preparation, source, properties, tests and assay, actions and therapeutic indications. Lists of specialties containing the subject drugs are included; for these specialties composition, available form and manufacturers are given. All drug names appear in the general alphabetic index. Publisher's address: Reichpietschufer 20, Berlin W.35.

Drogisten Lexikon; Ein Lehr- und Nachschlagebuch für Drogisten und Verwandte Berufe, Chemotechniker Laboranten, Grosshandel und Industrie, ed. by Dr. Hans Irion. Berlin, Springer- Verlag, 1955. Vols. 1 and 2 in 3 parts (1088, 1635 pp.) DM 68.—, DM 98.—. Volume 3 in prepn.

A comprehensive illustrated reference work on drugs and pharmaceutical practice. Volume 2 (in 2 parts, A-K and L-Z) contains monographs, alphabetically arranged, on drugs, chemicals, botanicals and other substances used in pharmacy. Drug monographs report composition, alternate names, description, properties, synthesis or source, actions, indications, precautions and sometimes tests and assays from the *Deutsches Arzneibuch.* The emphasis is on chemicals and botanic drugs; specialty drugs and combinations are infrequently mentioned and antibiotics are not included at all. Volume 1 consists of sections by named authors on subjects related to pharmacy; they include general pharmaceutical procedures, botany, chemistry, pharmacognosy, colors and dyes, toxicology, microscopy, photography, insecticides and their use (200 pages), surgical sundries and dressings, and tablets. The general alphabetic index includes all drug names. A bibliography of 273 books and 30 journals (all German) is in Volume 2, pp. 1460-1468. Publisher's address: Reichpietschufer 20, Berlin W.35.

Gehes Codex der Pharmazeutischen Spezialpreparäte, mit Angaben uber Zusammensetzung, Indikationen, Zubereitungsformen und Herstelle. 8th ed., compiled by Dr. Georg Otto. Stuttgart, Wissenschaftliche Verlagsgesellschaft, 1953. 927 pp. Approx. DM 80.—.

. . . . Supplement 1, 1954. 287 pp. DM 27.—
. . . . Supplement 2, 1956. 294 pp. DM 28.50

A comprehensive single-volume alphabetic list of drug specialties manufactured or sold in Germany, entered under proprietary names. Information about individual drugs includes composition, indications, how supplied and manufacturer's name and address. The year the drug was first marketed is frequently noted and trade names are indicated. Supplements are published with regularity and full revision takes place every few years. Publisher's address: Tübinger Strasse 53, Stuttgart 1.

Aufbietungsdatum. Frankfurt/Main, Arbeitsgemeinschaft der Berufsvertretungen Deutscher Apotheker. Cards 4″ by 6″.

This card service covers German specialties only, but it seems to cover the production of many manufacturers. Drugs are entered under proprietary name. Information includes composition, chemical structure, indications, administration, supply and dosage, manufacturer with address and sometimes literature references. The service is very prompt. Revised cards are mailed when new forms are introduced. An announcement is sent when drugs are discontinued. Cards are dated. Publisher's address: Platz der Republik 42, Frankfurt/Main.

Moderne Arzneimittel, by Burghard Helwig. Stuttgart, Wissenschaftliche Verlagsgesellschaft, 1956. 756 pp. DM 68.—.

As in its predecessor, *Neuere Arzneimittel,* drugs are arranged in *Moderne Arzneimittel* according to therapeutic indication. Each section is an alphabetic list of specialty drugs; for individual drugs information includes manufacturer, chemical composition (sometimes structural formula and properties), actions, specific indications, dosage and how supplied. There are a list of manufacturers with addresses and a general alphabetic index to all drug names. Publisher's address: Tübinger Strasse 53, Stuttgart 1.

Taschenbuch der Moderne Arzneibehandlung, by Dr. Gustav Kuschinsky. Stuttgart, Georg Thieme, 1956. 523 pp. DM 19.80.

This handbook for physicians has three principal sections. Section I is a therapeutic index which summarizes current drug therapy for the diseases listed. Section II is a pharmacologic index in which drugs are grouped according to their pharmacologic effects; a brief description of drug action, side effects, indications and contraindications accompanies each entry. Section III is an alphabetic list of drugs; for each entry is given manufacturer, composition, indications, dosage and supply. Specialties may be entered individually in the alphabetic list or listed as available forms under a common-name drug or a class of drugs (as *Reserpine, Röntgenkontrastmittel*). Cross references are used liberally, but there is no general index. Publisher's address: Thomaskirchhof 21 Postf. 535, Leipzig C.1.

Kartei der Praktischen Medizin, edited by Deutscher Kartei Verlag. Bad Salzuflen, Dr. Erich Mertinat & Co. Cards 4" by 6".

Essentially this is an abstract service for German medical and pharmaceutical journals; arrangement is by therapeutic indication. The indication appears at the upper left corner of the card, followed by a detailed abstract. An index card refers from proprietary names of drugs to indications under which will be found references to the use of these drugs.

Dental Pharmazeutisches Taschenrezeptierbuch, by Paul Brandau. 2d ed. Heidelberg, Dr. Alfred Hüthig Verlag, 1950. 516 pp. DM 14.—.

This handbook of dental drugs has two lists, one of drugs used in general practice, the other of drugs used especially for dental practice. Drugs in both lists are grouped according to indication, then listed alphabetically by common or proprietary name. Entries report name of manufacturer, composition, indications, uses, sizes and prices. A separate list of manufacturers is included. All drug names are included in the general alphabetic index. Publisher's address: Mönchhofstrasse 15, Heidelberg.

Europaische Drogen, by Heinz A. Hoppe. Hamburg, Cram, de Gruyter Co., 1948, 1951. 2 vols. (226, 378 pp.) DM 18.—, DM 25.50.

A two-volume illustrated reference work on medicinal plants, arranged alphabetically by plant name. General botanic information for each plant includes botanic name, description, cultivation and use. The medicinal forms are listed with statement of use, country of origin, production methods, description, constituents, therapeutic indications, commercial forms, variations, adulterations and assay. All plant names are included in the general alphabetic index, but not the names of oils, alkaloids, etc., extracted from them. Publisher's address: Messberghof 8, Hamburg 1.

Bundesverband der Pharmazeutischen Industrie. Rote Liste 1957: Verzeichnung Pharmazeutischer Spezialpräparate. Aulendorf/Württ., Editio Cantor. 864 pp. DM 15.—.

Entries in this price list for specialty drugs report composition, principal indications, dosage, available forms and package sizes, price to pharmacist and name of manufacturer. A list of manufacturers with their products is included.

Arzneimittel Kommission der Deutschen Ärzteschaft. Arzneiverordnungen; Ratschläge für Ärzte, edited by Dr. W. Koll and H. U. Kaller. 10th ed. Stuttgart, Hirzel Verlag, 1956. 387 pp. DM 12.—.

Includes new remedies, prices, list of specialties. Publisher's address: Birkenwaldstrasse 185, Stuttgart N.

Kleine Spezialitätentaxe. 12th ed. Deutscher Apotheker-Verlag. DM 10.—.

A price list giving wholesale and retail prices, package sizes, dispensing rules and name of manufacturer of common specialties. Publisher's address: Tübingerstrasse 53, Stuttgart 1.

East Germany

Entwicklung und Chemie der Heilmittel, by Dr. Josef Klosa. Berlin, Verlag Technik.

Band I. Pharmazeutika der Pflanzenwelt, 1952. 360 pp. DM 15.—

Band II. Vitamine, Hormone, Enzyme, Eiweisstoffe, 1953. 356 pp. DM 15.—

Band III. Synthetische Pharmazeutika, 1952. 336 pp. DM 16.—

Arzneimittel der Deutschen Demokratischen Republik, compiled by Fritz W. Joedecke. Berlin, Verlag Volk & Gesundheit, 1954. 408 pp. DM 16.—.

Arzneimittelverzeichnis. 2nd ed. Berlin, Verlag Volk & Gesundheit, 1955. 244 pp. DM 3.— (Ministerium für Gesundheitswesen).

Deutsche Arzneitaxe 1936; Nachdruck 1955. Berlin, Verlag Volk & Gesundheit, 1955. 140 pp. DM 5.30.

VETERINARY PRODUCTS

Handbuch der Tierärztlichen Praxis. Band II. Pharmakologie mit Tierarzneimittelverzeichnis. 7th ed., edited by G. Übele. Stuttgart, Verlag Medica, 1954. 731 pp. DM 98.—.

Tierarzneimittel-Rezepte, by G. Stather. Stuttgart, Wissenschaftliche Verlagsgesellschaft. 137 pp. Approx. DM 35.—.

Blaue Liste der Veterinarpharmazeutischen Erzeugnisse, by Dr. Pfutzner. Hamburg (Gärtnerstrasse 34).

Tierärztliche Arzneiverordnungen, by Konrad Ullrich. Terra-verlag Konstanz, 1952. 188 pp. DM 18.60.

Compiler's note: In response to the Committee's request for information about recent source books, our German correspondent forwarded a long list of publications of both East and West zones, not all of which could be examined before the deadline for this issue. Hence in certain areas where the need for information is very great, entries are submitted without annotation. A list of about fifteen indexes, price lists and therapeutic guides is retained for further checking.

The Committee on Drug Information Sources has the following members:

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A limited number of reprints are available for distribution by the Committee at 30¢ each. Requests should be sent to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J. Payment should accompany order.

Regular distribution will not be undertaken by the Section. Individuals and libraries wishing to ensure continued receipt of "Drug Information Sources" may do so by entering subscriptions to *American Journal of Pharmacy.*

Correspondence about "Drug Information Sources" should be directed to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J. (Ed.)

"SOAPINESS" IN "WHITE" CHOCOLATE CANDIES

By Bernard Witlin and Robert D. Smyth *

SINCE the introduction of chocolate as a confection, many attempts have been made to alter either the flavor or color of the product. In fact, many formulas imitating chocolate have been developed. Among the latter there has been a so-called "white" chocolate which was originally prepared with cocoa butter, rice flour, powdered milk and flavoring. Whereas the designation "white" chocolate is misleading and such preparations are considered adulterations of chocolate by the U. S. Food and Drug Administration, confectioners have now assigned such names to the product as "white coating", "bon-bon coating" and "fondant coating". In the past decade, "white" chocolates have gained consumer popularity especially as a summer confection. These contain cocoa butter, hydrolyzed vegetable oils, powdered whole milk, powdered skim milk, and emulsifying agents such as lecithin. As an ivory-colored confection, if desired, certified edible dyes can be added for a resulting variety of colors ("Rainbow" coatings).

In some instances where "white" chocolate had been employed as a coating, it was noted that during a normal shelf life, a "soapy" flavor developed in the confection. In a review of the literature we were unable to find any data dealing with such findings in candy. In this study the cause of such "soapiness" was investigated considering both the chemical and microbiological aspects.

A variety of "white" chocolate candies were purchased on the open market. They were organoleptically tested in order to separate the "soapy" from the normal candies. A sufficient quantity of the "soapy-tasting" candies was purchased to conduct our analyses.

Methods and Results

I—*Isolation of Microorganisms from "Soapy" Candy*

The "white" chocolate-coated candy was removed from the original store-wrapped container with sterile forceps and placed into a sterile Petri dish. The outer coating was then removed with sterile forceps and the centres were placed in another sterile Petri dish.

* Department of Bacteriology, Philadelphia College of Pharmacy and Science.

Small portions of the coatings and centres were emulsified in sterile water and inoculated onto the following media: (A) Sabouraud Dextrose Agar (slants), (B) Tryptone-Glucose-Yeast Extract Semi-Solid Agar (butt), (C) Tryptone-Glucose-Yeast Extract Agar (slants), and (D) A. P. H. A. Nutrient Agar (1) (plates). Incubation was carried out at temperatures of 22° C. and 34° C. for 48 hours. The organisms were then subcultured for isolation on media (A) and (D). They were then identified by biochemical methods as described in Bergey's Manual of Determinative Bacteriology (2). The following table is representative of the results obtained over a period of several months on "soapy" candies obtained from various sources.

TABLE I

ISOLATION OF MICROORGANISMS FROM "SOAPY" CHOCOLATE

Media	A	B	C	D
Temperature 22° C.	p, b	p, b	b	b
Temperature 34° C.	b	b	b, d	b, d

Legend:

b—Gram positive, spore-forming bacillus
d—*Sarcina lutea*, gram positive coccus
p—*Penicillium* species

The following chart is descriptive of the morphological and biochemical characteristics of the spore-forming bacillus:

Morphology by Gram's Method of Staining: spore-bearing rod. Gram stain was positive.
Endospores were central.
Agar colonies—white, spreading.
Rods—.7 to 1 microns by 2 to 3.5 microns; single or in short chains. On glucose nutrient agar fat globules were present in cell as noted by fat staining procedures.
Motility—positive.
Agar colonies—spreading, white, and dense with a smooth texture.
Broth—turbidity followed by pellicle formation.
Chromogenesis on agar—none.
Chromogenesis on potato medium—none.
Gelatin Liquefaction by stab method—positive.

Gelatin Liquefaction by Smith Modification of Frazier Method—positive.
Litmus milk—rapid proteolysis.
Indol Production—negative.
Urease—negative.
Lipase—positive.
Nitrate reduced to nitrite—positive.
Voges Proskauer—negative.
Growth at pH 6.0—negative.
Citrate—negative.
Blood agar—Beta hemolysis.
Acid in Dextrose, maltose, salicin, fructose, sucrose, trehalose and glycogen.
No reaction in lactose, xylose, mannitol, dulcitol, arabinose, esculin, erythriyol, sorbitol, adonitol, rhamnose, inositol.
Starch hydrolyzed to glucose.
Thermal Death Point—85° C. for 90 minutes.
Optimum Growth Temperature—34° C.
Minimum Growth Temperature—20° C.
Maximum Growth Temperature—55° C.

This organism resembles *Bacillus firmus* in both cultural and biochemical properties. A definite species was not assigned to the organism because of slight variances that existed between it and *B. firmus* as described by Bergey (2).

II—*Reproduction of "Soapiness" in "White" Chocolate Candies*

It was noted in this series of experiments that "soapiness" was found only in those candies possessing "white" chocolate coverings, and also that the spore-former was only found in the chocolate coating and not in the centers. Pieces of solid "white" chocolate bars which did not exhibit the "soapy" taste were treated in the following manner: (A) Coating surface with a saline suspension of spore-forming bacillus, (B) Intimate contact with "soapy" tasting "white" chocolate coating from candy, (C) Coating surface with a saline suspension of *Sarcina lutea,* and (D) Coating surface with a saline suspension of *Penicillium* species. The saline was 0.9% NaCl in distilled water. The material was placed in sterile Petri dishes and incubated at 22° and 34° C. for the below-mentioned time intervals. Organoleptic tests were made at one week intervals by removing small portions with a sterile scalpel. The results were as follows:

TABLE II

"SOAPINESS" IN "WHITE" CHOCOLATES (TEMPERATURE—22° C.)

Time (weeks)— Type Coating	1	2	3	4	5	6	7
A	O	O	O	O	S	S	S
B	O	S	S	S	S	S	S
C	O	O	O	O	O	O	O
D	O	O	O	O	O	O	O

Legend: (O) indicates the absence of a "soapy" taste; (S) indicates the presence of a "soapy" taste.

Samples incubated at 34° C. developed a "soapy" taste when coated with (A) and (B) type coatings three to five days later than the samples incubated at 22° C. It was observed that at the end of five weeks, the spore-forming bacillus produced enough "soapiness" to be organoleptically detectable. *Sarcina lutea* and *Penicillium sp.* had no effect on the candy, while the "soapy" candy contact coating reproduced the "soapiness" within two to three weeks. The time interval difference between the reproduction of "soapiness" in coatings (A) and (B) may be explained by the fact that in the latter this condition already existed thus making conditions more favorable for the reproduction of "soapiness" than in the former. It was noticed that "soapiness" developed only on the surface layer of thick bars of "white" chocolate. This surface reaction is indicative of an aerobic process. It was also noted that "soapiness" developed only in the "white" chocolate coating and not in the centers. The spore-forming bacillus was repeatedly found in all candies possessing the "soapy" taste. Therefore in this experiment, the bacteriological and biochemical properties of this organism were investigated further.

III—*Lipase Production by the Spore-Forming Bacilli*

Tests were performed to determine the lipolytic activity of the bacilli under investigation. The following procedure was used: (1) The fat was extracted from the chocolate candy by ethereal extraction and evaporation; (2) An emulsion of the fat in water was made and sterilized by inspissation at 70° C. for 30 minutes each day for four days; the emulsion was sub-cultured in Fluid Thioglycollate Medium (Difco) to check the sterility of the preparation. (3) Fat agar was prepared by mixing one ml. of the emulsion with ten ml. of agar at 45° C. (4) The organism was inoculated onto the surface of the agar plates and incubated at 22° and 34° C. for one week. The plates

were then flooded with a saturated solution of copper sulfate and allowed to remain in this solution for one hour at room temperature. Fatty acids are detected by the presence of a greenish opalescence around the edges of the colony (4). Lipase activity was demonstrated at both temperatures, and also on glyceryl mono-oleate, glyceryl mono-laurate, and on cetyl palmitate agars at both temperatures.

IV—*Quantitative Determination of Fatty Acid Production*

The next step was to determine quantitatively the extent of lipolytic action in terms of fatty acid production. The following method was used: One ml. of a saline emulsion of the bacilli was introduced into 5 ml. of the following media; Media #1—5% sterile fat emulsion (fat obtained from the chocolate coating), and Media #2—5% sterile fat emulsion (fat obtained as mentioned above) with 2% peptone and 1% yeast extract in sterile solution. Incubation was carried out at 22° and 34° C. The tubes were examined at 48 hour intervals and titrated with 0.0102N NaOH. One ml. of the media was titrated at the specified time intervals with the NaOH. The results were as follows:

TABLE III

FATTY ACID PRODUCTION BY ORGANISM ISOLATED FROM "SOAPY WHITE" CHOCOLATE

Media—	#1		#2		
Time (hours)	C	I	C	I	
0	0.5	0.5	3.0	3.0	Temperature—22° C.
48	0.5	0.5	5.8	6.0	
96	0.5	0.5	5.8	6.3	
144	0.5	0.75	5.8	7.5	
0	0.5	0.5	3.0	3.0	Temperature—34° C.
48	1.0	1.0	4.0	5.9	
96	2.0	2.0	4.7	5.9	
144	2.0	2.0	5.1	7.1	

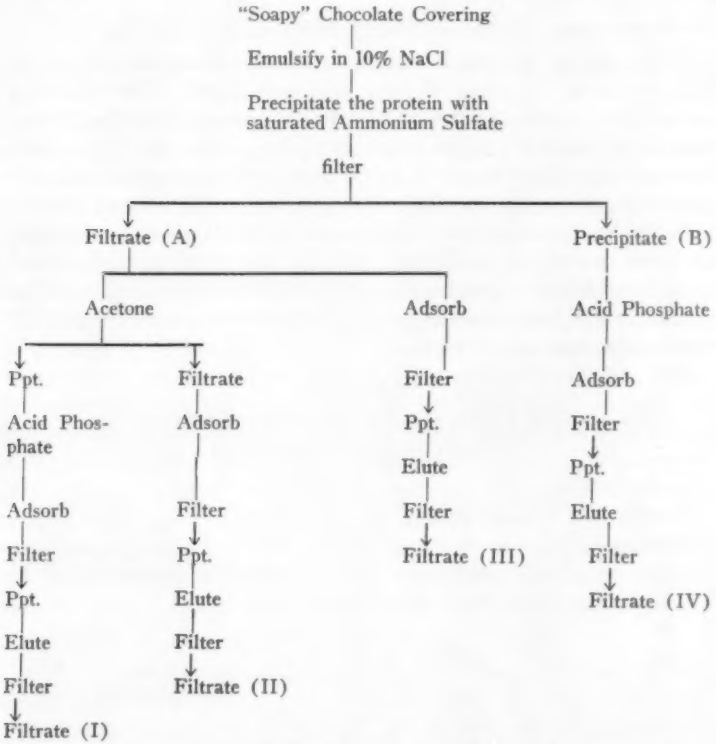
Legend: Results are expressed in terms of 0.0102 N NaOH required in ml. to neutralize one ml. of medium at the specified time interval. "(C)" indicates the uninoculated blank control, and "(I)" indicates the inoculated medium.

It was noted from the above results that more fatty acids were produced in the presence of nutrient material. In the absence of

nutrient material the concentration of fatty acids produced is negligible. In the presence of such material there is a definite difference between the control and the inoculated medium.

V—*Chemical Isolation of Various Enzyme Fractions*

Six enzyme fractions were isolated from chocolate candy possessing the "soapy" taste. The method used is as follows:



Note: The pH of the alkaline phosphate was 8.0 and the acid phosphate 6.0. Adsorption was obtained by mixing the substance with Filter-Cel and allowing the mixture to stand at room temperature for one hour in order to adsorb the enzyme or impurities as might have been the case. Elution was carried out by mixing the substance adsorbed on the Filter-Cel with alkaline phosphate, and shaking on an electrical reciprocating shaker for twenty to thirty minutes. The mixture was then filtered through ordinary filter paper by means of a suction apparatus. This enzymatic fractionation was also performed on white chocolate devoid of the soapy taste.

After the enzymes were isolated, the following six fractions were obtained:

A. Filtrate Enzyme

B. Precipitate Enzyme

I. Acetone Precipitate Enzyme

II. Acetone Filtrate Enzyme

III. Adsorbed Filtrate Enzyme

IV. Adsorbed Precipitate Enzyme

The enzymes were tested by the following method: Three ml. of fat emulsion (obtained as previously described) were added to one ml. of specific enzyme fraction, and the mixture was incubated at 22° and 34° C. The media were titrated with 0.0102 N NaOH at 48 and 96 hour intervals. One ml. of the media was titrated. Controls consisted of a 5% fat emulsion to which no enzyme had been added. The following chart represents the results of the enzyme fractions isolated from "soapy" chocolate:

TABLE IV

ACTIVITY OF ENZYMES ISOLATED FROM "SOAPY" WHITE CHOCOLATES

Temperature	Enzyme Fractions A	I	II	III	IV	Control	
22° C.	3.55	.75	.58	1.71	.17	.16	Time—48 hours
34° C.	3.50	1.67	1.30	1.67	.74	.75	
22° C.	5.55	1.05	1.26	3.71	.35	.42	Time—96 hours
34° C.	5.45	3.37	3.30	3.82	1.33	1.59	

Results are expressed in terms of 0.0102 N NaOH required to neutralize one ml. of medium.

Enzyme fractions were lipolytically active in the following order:

At 22° C.—A-III-II-I
At 34° C.—A-III-I-II

Since the activity of the control was greater than the activity of Fraction IV it was assumed that this fraction possessed no lipase activity.

The above results indicate that there was definitely present in the "soapy" candy several active enzyme fractions. This same display

of activity was exhibited by the spore-forming bacillus. The "white" chocolate devoid of the "soapy" taste exhibited no enzyme activity on the chocolate fat emulsion.

An investigation of the basic ingredients employed in the manufacture of "white" chocolate revealed that similar spore-forming rods are present in powdered skim milk produced under poor sanitary conditions. These organisms are usually present in the soil and air and enter such milk as contaminants prior to or during processing. Fettick (3) reported the presence of *Bacterium saprolacticum* in milk possessing a "soapy" taste, and upon isolating the bacteria reproduced this effect in sterile milk. Organisms of the genera *Pseudomonas* (5-7) and *Bacillus* (8-10) have been reported in association with the production of a "soapy" taste in dairy products.

Summary and Conclusions

A spore-forming, gram-positive bacillus was isolated from "soapy white" chocolates and was shown to possess lipolytic activity with the production of fatty acids. The organism was identified as being closely related to *Bacillus firmus*. This organism was repeatedly isolated from "soapy white" chocolates. Enzyme fractions were obtained from the "soapy" chocolates and displayed lipolytic activity as did the sporulating bacillus. "Soapiness" was reproduced in candy devoid of the "soapy" taste by inoculation with the bacillus and also by contact with "soapy" candy. It was concluded that this organism was the etiological agent of "soapiness" in "white" chocolates.

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A NOTE ON THE SENSITIVITY OF AN EQUAL-ARM BALANCE

By Robert N. Jones

RECENTLY, while writing up an explanation of the theory concerning the sensitivity of the analytical balance, the author was corrected by Dr. Thomas D. Cope who suggested that a careful study be made of the subject. Because friends of the writer, both chemists and physicists, all had the same wrong concept, this article has been prepared.

The popular concept is that the sensitivity of an equal-arm balance decreases with load but this is not necessarily true.

The sensitivity of an equal-arm balance depends upon the length of the equal arms, the mass of the beam and pointer, the location of the center of gravity of the beam and pointer, and the weights of the pans and load if the three knife-edges are not coplanar.

Referring to Figure I the beam of length 2L rocks on the knife-edge O and supports the pans on knife-edges A and B. At O is a downwardly projecting pointer OD, the lower end of which swings back and forth across a scale. The center of gravity of the beam and pointer of mass M should be located at some point C along the pointer, a distance d below O. If the knife-edges at A and B are not coplanar with knife-edge O, let h represent the height of A and B above knife-edge O when the beam is horizontal. The broken lines represent the beam and pointer when not deflected, and the solid lines show the result of adding a small unbalancing mass p to one of the scale pans, producing angle Θ. The equal masses on each side, including mass of pan and load before p is added, are represent by m.

The addition of mass p sets up a deflecting torque about O equal to $(m + p)g(L \cos \Theta + h \sin \Theta)$ which becomes smaller and smaller as Θ increases. At the same time, Mg is displaced producing an opposite torque about O equal to $Mgd \sin \Theta$ which becomes larger and larger as Θ increases. Also, if the three knife-edges are not coplanar a torque $mg(L \cos \Theta - h \sin \Theta)$ develops. The beam and pointer will come to rest when Θ has such a value that

$(m + p)g(L \cos \Theta + h \sin \Theta) = Mgd \sin \Theta + mg(L \cos \Theta - h \sin \Theta)$

Simplifying $(Md - 2mh) \sin \Theta = pL \cos \Theta + ph \sin \Theta$

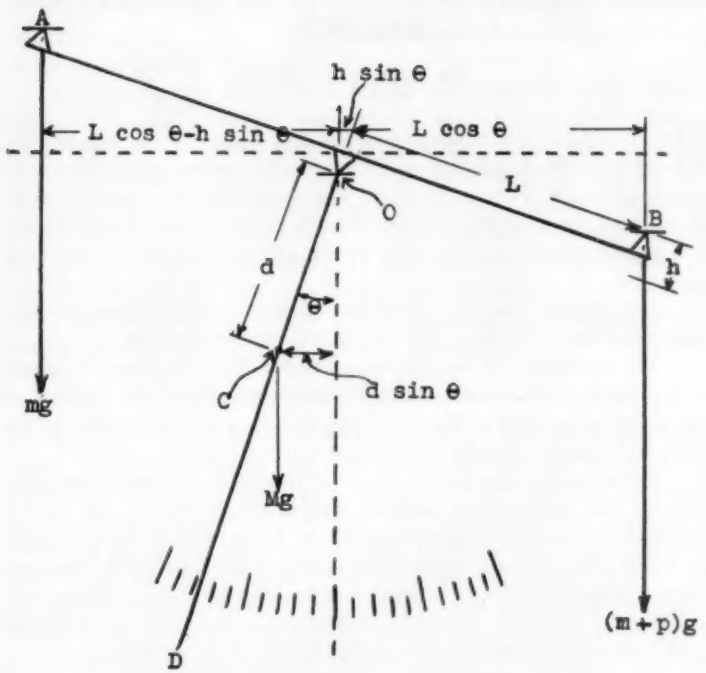

FIGURE I. THE ANALYTICAL BALANCE

2L is the length of the beam
O is the center of the beam and central knife-edge
OD is the pointer
C is the center of gravity of the beam and pointer
mg is the weight of each pan and load on the pan
pg is the small unbalancing weight
Θ is the angle of deflection produced by pg
h is the height of knife-edges A and B above knife-edge O
Mg is the weight of the beam and pointer

For small values of Θ the last term can be neglected usually because p, h, and sin Θ are all small and the product of the three is even smaller.

A sensitive balance is one which sweeps through a large angle when a very small unbalancing mass is added to one scale-pan, and

the sensitivity is commonly expressed as the number of scale divisions the pointer is deflected per milligram of unbalancing mass. Physically, however, the sensitivity is defined from the previous equation. While the ratio of the number of scale divisions per milligram cannot be expressed directly from the equation, the ratio of tan Θ per milligram can be. Dropping the last term as already mentioned and dividing both sides of the equation by (Md — 2mh) p cos Θ, the following results:

$$\frac{\sin \Theta}{p \cos \Theta} = \frac{L}{Md - 2mh} \quad \text{and} \quad \frac{\tan \Theta}{p} = \frac{L}{Md - 2mh}$$

Also, when the knife-edges are all coplanar, h equals zero and

$$\frac{\tan \Theta}{p} = \frac{L}{Md}$$

Thus, if the three knife-edges are coplanar the sensitivity of an equal-arm balance is independent of the masses of the pans and load. If A and B are above O the sensitivity increases with load, and *only if A and B are below O,* does the sensitivity decrease with increased load.

Several good references are:

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Newman, F. H. and Searle, V. H. L. *The General Properties of Matter* (New York: The Macmillan Company, 1929), pp. 16-17.

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SELECTED ABSTRACTS

The Clinical Significance of Weight Trends During Pregnancy. Thomas, A. M., and Billewicz, W. Z. *Brit. Med. J.* No. 5013:243 (1957). A series of 4,214 cases of primigravida were analyzed with regard to the relationship of changes in weight to complications of pregnancy. Multigravidae were excluded because these patients are less likely to develop complications. The cases selected were all primigravidae registered in one hospital over a six-year period where records were adequate. These patients had not been subject to weight regulation. The incidence of pre-eclampsia, prematurity and prenatal death among these cases was similar to the usual incidence of these complications.

The analysis showed that the average gain of weight was greater among patients developing pre-eclampsia than among those with normal pregnancies. It was also evident that the incidence of pre-eclampsia was greater as the rate of weight gain increased. However, these facts are not reliable for predicting pre-eclampsia in the individual case.

The incidence of prematurity was found to be highest when weight gains were consistently low. The incidence was lower when the rate of weight gain was about normal and increased when the rate of weight gain was high. The complication of pre-eclampsia was found to be a significant cause of prematurity in the high weight gain group but not in the low weight gain group.

The most favorable outcome of pregnancy with respect to pre-eclampsia, prematurity and prenatal death was associated with a moderate rate of weight gain. This rate of weight gain was about 1 lb. a week from the 20th to 30th week of gestation and a slightly lower rate thereafter.

An attempt to provide control of weight gain in pregnancy has been undertaken by the authors. The full control and evaluation of such a program is difficult. Data is not yet available from this study. It is not yet possible to predict whether or not such a program will reduce the incidence of the complications of pregnancy.

A Presumptive Method for Differentiating Bacterial From Viral Pharyngitis and Tonsilitis. Green, M. H. *U. S. A. F. Med. J. 8:180* (1957). On the basis of clinical observation it is not always easy to differentiate pharyngitis and tonsilitis of bacterial origin from that of viral origin. In the northeastern section of the United States it is estimated that approximately 75 per cent of these cases are of viral origin with the remainder probably largely caused by beta-hemolytic streptococcus. In the latter conditions, penicillin is usually effective in rapidly controlling the infection but not in the former cases. Culture techniques for identifying the causative agent require serious delay in beginning therapy.

The author described a simple presumptive test for differentiating the two types of infection. A cotton swab was applied to the inflamed area of the throat and then rolled over a glass slide. The slide was then stained with Wright's Stain and examined microscopically for the predominate cell. If the cells were predominately neutrophilic or eosinophilic leukocytes, the infection was almost always bacterial in origin. If the cells were predominantly monnuclear, the infection was almost always viral in origin.

The author pointed out that a source of error in the method was that late stages of viral infections, such as the common cold, were often characterized by a leukocytic response in the throat exudate. The authors attempted to overcome this error by studying cases within 24-36 hours after onset.

The author reported that in 26 cases with polymorphonuclear neutrophils predominate in the exudate examined by the presumptive test technique, 22 showed positive cultures for beta-hemolytic streptococci and 4 showed cultures for hemolytic staphylococci. Penicillin was administered in an intramuscular dose of 60,000 units to all of these patients immediately after the presumptive examination, again after 24 hours, and again after 96 hours. Response was rapid and complete within 12-36 hours in the patients with streptococcic infections. Good results were also obtained in the 4 patients with staphylococcic infections.

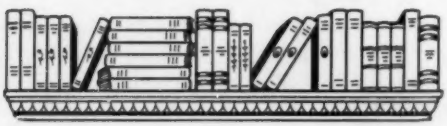
In 13 patients with mononuclear cells predominate in their exudate, no bacteria were obtained on culturing. Pencillin, administered to 7 right after the presumptive test, was ineffective. The author suggested that this presumptive test method warrants further study as a means of differentiating bacterial from viral pharyngitis and tonsilitis.

BOOK REVIEW

Heterocyclic Compounds, Volume VI. Edited by Robert C. Elderfield. John Wiley and Sons, Inc., New York 16, N. Y. 1957. vii + 753 pp. Price $25.00.

The subject of this volume of the well known series is six membered heterocycles containing two hetero atoms and their benzo derivatives. The contents include monocyclic diozanes, benzodioxanes, sulfur analogs of dioxanes, pyridazines, cinnolines and related compounds, phthalazines, pyrimidine and derivatives, quinazoline, pyrazines and piperazines, quinoxalines, monocyclic oxazines, benzoxazines, thiazines and benzothiazines, phenazines, phenoxazines and phenothiazines. The bibliographies for all the subjects include references up to 1955. While the index is still not adequate for a work of this scope, this book should be a great asset to any organic chemistry library.

A. R. GENNARO



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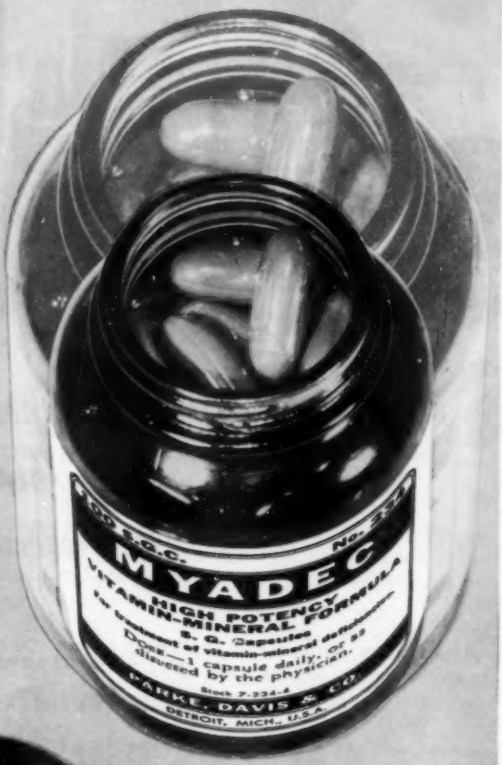

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